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ORIGINAL RESEARCH

Clinical Characteristics, Management Strategies, and Outcomes of Non–ST-Segment–Elevation Myocardial Infarction Patients With and Without Prior Coronary Artery Bypass Grafting

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BACKGROUND: There are limited data on the management strategies, temporal trends and clinical outcomes of patients who present with non–ST-segment–elevation myocardial infarction and have a prior history of CABG.

METHODS AND RESULTS: We identified 287 658 patients with non–ST-segment–elevation myocardial infarction between 2010 and 2017 in the United Kingdom Myocardial Infarction National Audit Project database. Clinical and outcome data were analyzed by dividing into 2 groups by prior history of coronary artery bypass grafting (CABG): group 1, no prior CABG (n=262 362); and group 2, prior CABG (n=25 296). Patients in group 2 were older, had higher GRACE (Global Registry of Acute Coronary Events) risk scores and burden of comorbid illnesses. More patients underwent coronary angiography (69% versus 63%) and revascularization (53% versus 40%) in group 1 compared with group 2. Adjusted odds of receiving inpatient coronary angiogram (odds ratio [OR], 0.91; 95% CI, 0.88–0.95; $P<0.001$) and revascularization (OR, 0.73; 95% CI, 0.70–0.76; $P<0.001$) were lower in group 2 compared with group 1. Following multivariable logistic regression analyses, the OR of in-hospital major adverse cardiovascular events (composite of inpatient death and reinfarction; OR, 0.97; 95% CI, 0.90–1.04; $P=0.44$), all-cause mortality (OR, 0.96; 95% CI, 0.88–1.04; $P=0.31$), reinfarction (OR, 1.02; 95% CI, 0.89–1.17; $P=0.78$), and major bleeding (OR, 1.01; 95% CI, 0.90–1.11; $P=0.98$) were similar across groups. Lower adjusted risk of inpatient mortality (OR, 0.67; 95% CI, 0.46–0.98; $P=0.04$) but similar risk of bleeding (OR,1.07; CI, 0.79–1.44; $P=0.68$) and reinfarction (OR, 1.13; 95% CI, 0.81–1.57; $P=0.47$) were observed in group 2 patients who underwent percutaneous coronary intervention compared with those managed medically.

CONCLUSIONS: In this national cohort, patients with non–ST-segment–elevation myocardial infarction with prior CABG had a higher risk profile, but similar risk-adjusted in-hospital adverse outcomes compared with patients without prior CABG. Patients with prior CABG who received percutaneous coronary intervention had lower in-hospital mortality compared with those who received medical management.

Key Words: coronary artery bypass grafting ■ mortality ■ non–ST-segment–elevation myocardial infarction ■ percutaneous coronary intervention

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CLINICAL PERSPECTIVE

What Is New?

- Patients with prior coronary artery bypass grafting (CABG) are older, with greater comorbid burden and present with higher GRACE (Global Registry of Acute Coronary Events) score compared with patients with no prior history of CABG.
- Once differences in baseline characteristics and presentation were adjusted for, we observed similar odds of inpatient mortality, major adverse cardiovascular events, reintervention, and major bleeding between the 2 groups.
- Sensitivity analysis of the prior CABG patients who received percutaneous coronary intervention showed they had better-adjusted clinical outcomes for in-hospital all-cause mortality compared with those who received medical management, despite the observation that patients with prior CABG were less likely to receive invasive management.

What Are the Clinical Implications?

- Percutaneous coronary intervention was underused in patients with non–ST-segment–elevation myocardial infarction who had a prior history of CABG, though it was associated with mortality benefit compared with conservative management.
- These results may provide insight to clinicians around the utility of an invasive management approach in this high-risk and complex cohort of patients.
- Prospective, randomized, controlled clinical trials are now needed to test the validity of these observational results.

Nonstandard Abbreviations and Acronyms

ACUITY	Acute Catheterization and Urgent Intervention Triage Strategy
GRACE	Global Registry of Acute Coronary Events
LIPSIA-NSTEMI	Leipzig Immediate Versus Early and Late Percutaneous Coronary Intervention Trial in NSTEMI
MACE	major adverse cardiovascular event
MINAP	Myocardial Infarction National Audit Project
OASIS-5	Organization to Assess Strategies in Ischemic Syndromes–5
RITA3	Randomized Intervention Trial of Unstable Angina 3
SVG	saphenous vein graft
TIMI	Thrombolysis in Myocardial Infarction

Coronary artery bypass grafting (CABG) is a commonly used revascularization strategy for the management of advanced coronary artery disease.[1,2] Graft failure is not uncommon, with occlusive disease of saphenous vein grafts (SVGs) affecting approximately two-thirds of patients within 10 years of surgery.[3–5] Bypass grafting accentuates the development of atherosclerosis, thrombosis, and calcification in native coronary arteries.[6–9] Consequently, occlusion of SVG and progression of native coronary artery disease are associated with the medium- and long-term risk of recurrent ischemic events, including myocardial infarction (MI).

Current European and American guidelines provide a class 1 recommendation for an early invasive approach in high-risk patients with non–ST segment elevation MI (NSTEMI) based on the results of 10 randomized trials, which compared invasive versus medical management.[10–13] However, many of these key trials[14–17] did not include patients with prior CABG or only recruited small numbers of such patients. Previous evidence derived from observational data has revealed that an invasive strategy is less likely to be adopted in patients with NSTEMI with prior CABG,[17–20] and when coronary angiography is undertaken, these patients are less likely to receive revascularization. Clinical outcome data in this cohort are inconsistent. For example, in a post hoc analysis of the ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) trial, adjusted 30-day and 1-year risk of major adverse cardiovascular events (MACEs) was higher in patients with prior CABG who underwent revascularization compared with those who were treated conservatively.[18] In contrast, in a Swedish registry of 10 837 patients with prior CABG, 1-year adjusted mortality was 50% lower in those who received revascularization compared with those who received medical management.[21] No randomized controlled trial has exclusively examined the outcomes of this patient cohort in NSTEMI,[22] although in a pilot trial of 60 patients, medically stabilized patients with NSTEMI with a prior history of CABG were randomly assigned to invasive or medical management. Similar clinical outcomes were reported in the 2 treatment strategies, although the sample size was inadequate to draw conclusions about the effectiveness of an invasive strategy. Therefore, the optimal management strategy in patients with prior CABG who present with NSTEMI is not clearly defined. Hence, this study aimed

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to (1) investigate management strategies and clinical outcomes of patients presenting with NSTEMI with a history of prior CABG in contemporary clinical practice and (b) analyze the association of an invasive approach to in-hospital clinical outcomes using the data from the Myocardial Infarction National Audit Project (MINAP) in the United Kingdom.

METHODS

Study Settings

This analysis is based on the data derived from MINAP, a comprehensive, national clinical registry of patients hospitalized with type 1 MI in England and Wales.[23,24] The MINAP data set consists of 130 variables and records information about patients with acute MI including baseline clinical characteristics, comorbid conditions, management strategies including invasive and conservative, pharmacotherapy, place of care, in-hospital clinical outcomes, and diagnosis on discharge. Data are submitted by hospital clinical and clerical staff, and pseudorandomized records are uploaded to the National Institute for Cardiovascular Outcomes Research central database. Two hundred six hospitals enter over 92 000 new cases to MINAP annually, and approximately 1.5 million patient records are currently present in this database. Institutional research and ethical board approval were not required for this study, as all data were anonymized and routinely collected as part of the national audit. Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the National Institute for Cardiovascular Outcomes Research at nicor.helpdesk@nhs.net.

Study Design

This is a retrospective analysis of prospectively collected data of patients admitted with a diagnosis of NSTEMI in England and Wales between January 1, 2010, and December 31, 2017. The discharge diagnosis of NSTEMI was decided by treating clinicians according to presenting complaints, clinical examination, and the results of in-hospital investigations in keeping with the European Society of Cardiology guidelines.[25] Patients with missing data for prior history of CABG, mortality, and any individual patient with second or later admissions were excluded from analysis (Figure 1). This constituted a final cohort of 287 658 patients with NSTEMI, which were then categorized into 2 groups according to history of CABG: group 1, patients with no prior history of CABG; and group 2, patients with prior CABG. Clinical outcomes of interest were in-hospital all-cause mortality, reinfarction, major bleeding, and MACEs. MACE was defined as a composite end point of inpatient death or reinfarction. Major bleeding was defined as a composite of gastrointestinal, retroperitoneal, and intracranial hemorrhage. Patient risk assessment was performed using the TIMI (Thrombolysis in Myocardial Infarction) and GRACE (Global Registry of Acute Coronary Events) scoring systems.[26–28]

Statistical Analysis

Descriptive statistical analyses were performed to compare differences in baseline demographics, clinical characteristics, and crude adverse outcomes between the 2 cohorts. Continuous variables are presented as means and SDs and categorical variables by proportions. The chi-squared test and Student's *t* test were used to assess statistical differences between the 2 groups, in categorical and continues variables,

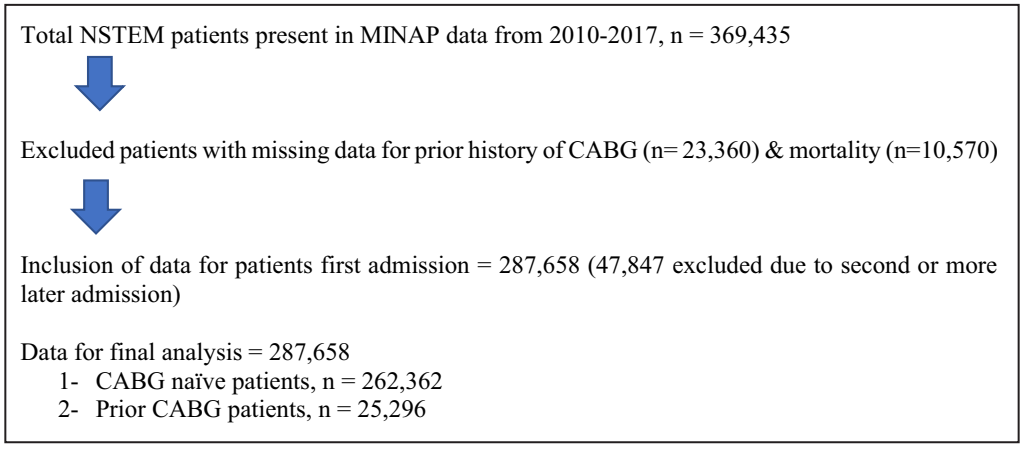

Figure 1. Consolidated Standards of Reporting Trials diagram to show to show all participant inclusion and exclusion.
CABG indicates coronary artery bypass grafting; MINAP, Myocardial Infarction National Audit Project; and NSTEMI, non–ST-segment–elevation myocardial infarction.

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respectively. We undertook multiple imputations with chained equation techniques to impute data for all variables with missing data.[29] We applied multivariable logistic regression analysis first on complete case analysis and then on imputed data sets to estimate the risk of adverse outcomes between groups. Estimates were combined using Rubin's rules.[30] Logistics regression models were fitted using maximum likelihood estimation and were adjusted for those variables that contributed significantly to adverse outcomes and had a *P* value <0.05 by using backward selection method. In multivariable analyses, we adjusted for age, sex, race, heart rate, blood pressure, body mass index, serum creatinine level, family history of coronary artery diseases, ischemic ECG changes, left ventricular systolic dysfunction, prior percutaneous coronary intervention (PCI), comorbid conditions (history of diabetes mellitus, hypercholesterolemia, angina, cerebrovascular accident, peripheral vascular disease, hypertension, smoking, admission under cardiology, pharmacotherapy (prescription of unfractionated heparin, intravenous nitrate, furosemide, mineralocorticoid receptor antagonist, beta blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor blockers, aspirin, P2Y12 inhibitor, statins), Killip class, cardiac arrest, cardiogenic shock, pulmonary edema, and procedures and investigations including coronary angiogram and PCI undertaken during admission.

In a sensitivity analysis, we used propensity score matching with the imputed data, to estimate the average treatment effects. We matched the 2 groups on the same variables used in the multivariable statistical analyses. One-to-one nearest-neighbor matching with replacement was applied, followed by logistic regression analysis (the sole predictor being group membership) to obtain the average treatment effects over the multiple imputed data sets. The coefficients were converted to odds ratios to allow for comparisons with the main analysis.

All statistical analyses were performed with Stata 14.2 (College Station, TX). All statistical analyses were 2-tailed, and an alpha of 5% was used throughout.

RESULTS

Our study cohort consisted of 287 658 patients who were admitted in England and Wales from January 2010 to December 2017 with a diagnosis of NSTEMI, of which 25 296 (9%) had a prior history of CABG. The process of patients' inclusion and exclusion for this analysis is presented in Figure 1. The annual proportion of patients with prior CABG during the study period ranged from 8.36% (2010) to 9.56% (2016) (*P*<0.001) (Figure 2).

Differences in baseline clinical characteristics between the 2 groups are presented in Table 1. Patients with prior CABG were significantly older, less likely to be women and White, but more likely to present with acute heart failure symptoms. The proportion of patients with a high-risk GRACE score (>140) was significantly higher in patients with prior CABG compared with patients without prior CABG (88% versus 76%; *P*<0.001). Furthermore, patients with prior CABG had a higher prevalence of comorbid conditions such as diabetes mellitus, congestive heart failure, chronic renal failure, hypercholesterolemia, previous MI and PCI, angina,

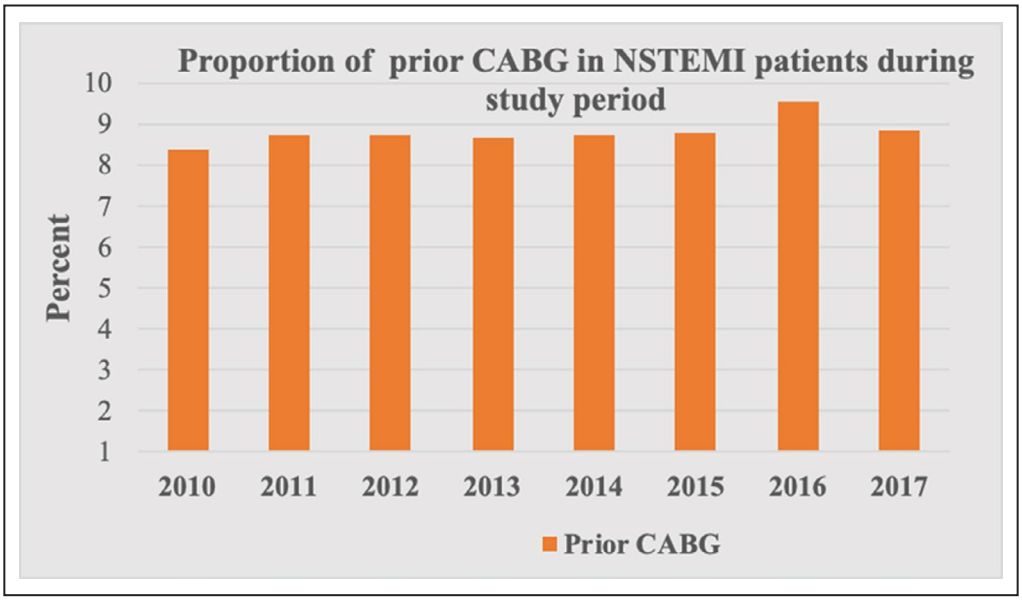

Figure 2. Proportion of prior CABG in total patients with NSTEMI during study period.
CABG indicates coronary artery bypass grafting; and NSTEMI, non–ST-segment–elevation myocardial infarction.

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Table 1. Clinical Characteristics

Variables	CABG Naïve (n=262 362)	Prior CABG (n=25 296)	*P* Value
Mean age, y (SD)	71 (14)	74 (10)	<0.0001
Women, n/N (%)	98 641/262 362 (38)	5249/25 296 (21)	<0.001
White, n/N (%)	221 796/240 353 (92)	20 955/23 342 (90)	<0.001
Mean body mass index, n (SD)	28 (8)	28 (8)	0.16
Race			
White (%)	221 796/240 353 (92%)	20 955/23 342 (90%)	<0.001
Black (%)	2420/240 353 (1%)	168/23 342 (1%)	
Asian (%)	12 921/240 353 (6%)	1882/23 342 (8%)	
Mixed (%)	3216/240 353 (1%)	337/23 342 (1%)	
Killip class			
No heart failure, n/N (%)	131 283/169 808 (77)	11 727/16 398 (72)	<0.001
Basal crepitations, n/N (%)	27 326/169 808 (16)	3468/16 398 (21)	<0.001
Pulmonary edema, n/N (%)	10 215/169 808 (6)	1090/16 398 (7)	0.001
Cardiogenic shock, n/N (%)	984/169 808 (0.58)	113/16 398 (0.69)	0.08
GRACE score, n/N (%)			
High-risk GRACE score >140	125 852/164 912 (76)	13 887/15 855 (88)	<0.001
Intermediate-risk GRACE score 109–140	31 338/164 912 (19)	1673/15 855 (11)	<0.001
Low-risk GRACE score <109	7722/164 912 (5)	295/15 855 (2)	<0.001
Other clinical characteristics			
ECG ST changes, n/N (%)	198 810/255 910 (78)	19 448/24 642 (79)	<0.001
Previous smoker, n/N (%)	89 504/250 038 (36)	11 778/23 908 (49)	<0.001
Current smoker, n/N (%)	57 514/250 038 (23)	2772/23 908 (12)	<0.001
Chronic renal failure, n/N (%)	21 299/260 091 (9)	3712/24 772 (15)	<0.001
Prior percutaneous coronary intervention, n/N (%)	30 157/261 618 (12)	7274/24 757 (29)	<0.001
Diabetes mellitus, n/N (%)	62 559/260 248 (24)	10 412/25 048 (42)	<0.001
Congestive heart failure, n/N (%)	18 330/260 050 (7)	3678/24 707 (15)	<0.001
Hypercholesterolemia, n/N (%)	87 740/257 531 (34)	11 875/24 575 (48)	<0.001
Previous MI, n/N (%)	62 226/201 068 (27)	16 242/24 857 (65)	<0.001
Angina, n/N (%)	68 358/259 721 (28)	16 877/24 764 (68)	<0.001
Cerebrovascular disease, n/N (%)	25 500/260 508 (10)	3476/24 814 (14)	<0.001
Peripheral vascular disease, n/N (%)	12 589/259 581 (5)	2686/24 685 (11)	<0.001
Hypertension, n/N (%)	141 155/260 496 (54)	15 943/24 981 (64)	<0.001
Asthma/COPD, n/N (%)	45 571/260 574 (17)	4 496/24 833	0.02
Family history of CAD, n/N (%)	60 829/219 8550 (28)	5447/19 992 (27)	0.20
Admission under cardiologist, n/N (%)	127 559/251 037 (51)	11 939/24 257 (49)	<0.001
Mean heart rate, bpm (SD)	82 (22)	79 (22)	<0.001
Mean systolic blood pressure (SD)	141 (28)	140 (28)	<0.001
Moderate LVSD (EF 35%–45%), n/N (%)	36 027/206 989 (17)	4741/19 996 (24)	<0.001
Severe LVSD (EF <35%), n/N (%)	14 820/206 989 (7)	2211/19 996 (11)	<0.001
Cardiac arrest, n/N (%)	8574/256 647 (3)	986/24 806 (4)	<0.001

CABG indicates coronary artery bypass grafting; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; GRACE, Global Registry of Acute Coronary Events; LVSD, left ventricular systolic dysfunction; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

cerebrovascular accident, peripheral vascular disease, hypertension, asthma/chronic obstructive pulmonary disease, and severe left ventricular systolic dysfunction.

Pharmacotherapy, management strategies, and unadjusted crude clinical outcomes for both cohorts are presented in Table 2. The proportion of patients who

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Table 2. Management Strategy and Crude Clinical Outcome

Variables	CABG Naïve (n=262 362)	Prior CABG (n=25 296)	*P* Value
Pharmacotherapy, n/N (%)			
Low-molecular-weight heparin	123 578/237 006 (52)	11 680/22 707 (51)	0.04
Fondaparinux	112 159/238 046 (47)	10 079/22 764 (44)	<0.001
Warfarin	14 064/235 919 (6)	2626/22 606 (12)	<0.001
Unfractionated heparin	33 108/235 250 (14)	2849/22 516 (13)	<0.001
Glycoprotein 2b/3a inhibitor	7428/239 183 (3)	702/22 919 (3)	0.72
Intravenous nitrate (%)	29 994/235 872 (12.7)	3010/22 600 (13.3)	0.01
Furosemide	64 962/236 401 (27)	9483/22 730 (42)	<0.001
Calcium channel blockers	43 849/236 045 (19)	6025/22 672 (27)	<0.001
Intravenous beta blockers	2744/237 066 (1)	237/22 700 (1)	0.12
MRA	15 261/234 348 (7)	2699/22 455 (12)	<0.001
Thiazide diuretics	11 300/235 555 (5)	1139/22 531 (5)	0.08
Aspirin	252 745/261 627 (97)	24 333/25 241 (96)	0.09
P2Y12 inhibitor	239 070/261 265 (91.5)	23 190/25 203 (92.1)	0.006
Statins	212 980/260 937 (82)	22 898/25 193 (91)	<0.001
ACE inhibitors/ARB	211 428/261 158 (81)	21 176/25 200 (84)	<0.001
Beta blockers	212 043/259 831 (82)	20 763/25 115 (83)	<0.001
Management strategy, n/N (%)			
Radionuclide study	5740/235 950 (2)	782/22 697 (3)	<0.001
Exercise test	8953/239 578 (4)	742/23 033 (3)	<0.001
Coronary angiogram	174 184/250 859 (69)	15 133/24 129 (63)	<0.001
PCI	90 717/202 853 (45)	7503/19 248 (39)	<0.001
CABG	16 350/202 853 (8)	269/19 248 (1.4)	<0.001
Revascularization (CABG/PCI)	107 067/202 853 (53)	7772/19 248 (40)	<0.001
Crude in-hospital clinical outcomes, n/N (%)			
Death	14 075/262 362 (5.4)	1291/25 296 (5.1)	0.08
Cardiac mortality	10 899/262 362 (4.15)	1079/25 296 (4.27)	0.40
Reinfarction	2205/250 647 (0.9)	273/24 152 (1.1)	<0.001
Major bleeding	4076/257 766 (1.58)	422/24 878 (1.7)	0.17
MACE*	15 749/262 362 (6)	1516/25 296 (6)	0.95

ACE indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CABG, coronary artery bypass grafting; MACE, major adverse cardiovascular event; MRA, mineralocorticoid receptor antagonist; and PCI, percutaneous coronary intervention.

*MACE is defined as composite end point of inpatient death and reinfarction.

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received furosemide (42% versus 27%; *P*<0.001) was markedly higher in the prior CABG group, reflecting the greater proportion of patients with HF in this cohort. The proportion of patients who received an invasive coronary angiogram (63% versus 69%; *P*<0.001), PCI (39% versus 45%; *P*<0.001), and CABG (1% versus 8%; *P*<0.001) were significantly lower in patients with a history of CABG.

Temporal Changes

In a temporal analysis to assess PCI during the study period, we observed an increase in PCI over time in group 1 (no prior CABG) (*P* for trend <0.001) and Group 2 (prior CABG) cohorts (*P* for trend <0.001) (Figure 3).

Clinical Outcomes in Patients Without Prior CABG Versus Patients With Prior CABG

The prevalence of in-hospital all-cause mortality (5.4% versus 5.1; *P*=0.08), major bleeding (1.58% versus 1.7%; *P*=0.17), MACE (6% in each group; *P*=0.95) were similar in both cohorts, but reinfarction was higher in patients with prior CABG (1.1% versus 0.9%; *P*<0.001). After adjustment for differences in baseline clinical and treatment characteristics, odds of all-cause mortality (OR, 0.96; 95% CI, 0.88–1.04; *P*=0.31), reinfarction (OR, 1.02; 95% CI, 0.89–1.17; *P*=0.78), major bleeding (OR, 1.01; 95% CI, 0.90–1.11; *P*=0.98), and inpatient MACE (OR, 0.97; 95% CI, 0.90–1.04; *P*=0.44) were similar between the 2 groups (Table 3).

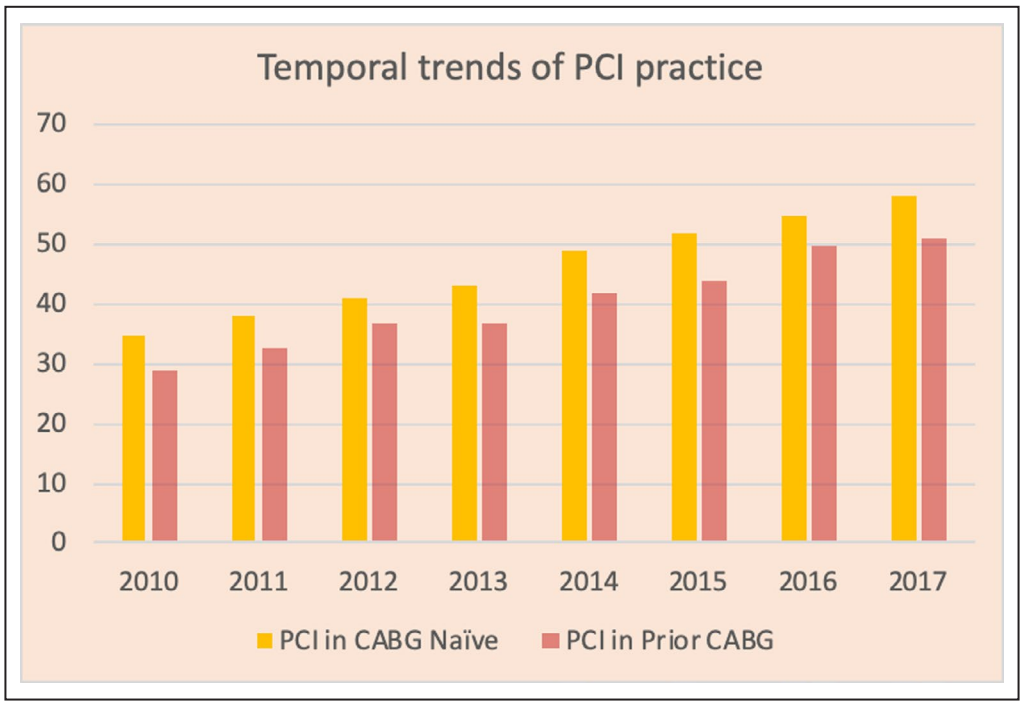

Figure 3. Temporal trends of PCI practice from 2010 to 2017.
P for trend PCI in patients with prior CABG < 0.001. *P* for trend for PCI in CABG-naïve patients < 0.001. CABG indicates coronary artery bypass grafting; and PCI, percutaneous coronary intervention.

Analysis With Propensity Score Matching

In a propensity score matching analysis, the adjusted risk of mortality during index admission (OR, 0.98; 95% CI, 0.83–1.14; *P*=0.82), in-hospital reinfarction (OR, 1.27; 95% CI, 0.82–1.72; *P*=0.24), in-hospital major bleeding (OR, 0.92; 95% CI, 0.69–1.14; *P*=0.47), and in-patient MACE (OR, 1.03; 95% CI, 0.87–1.20; *P*=0.67) were similar between the 2 groups (Table 4).

Table 3. Risk of in-Hospital Adverse Outcomes Following Multivariate Adjustments

Clinical Outcomes	Adjusted OR† as Compared With Reference (CABG Naïve)	*P* Value	95% CI
Complete case MV analyses			
Death* (no. of observations=92 266)	1.003	0.97	0.86 to 1.17
Reinfarction* (n of observations=90 558)	OR: 1.06	0.67	0.81 to 1.39
Major bleeding* (no. of observations=91 383)	1	1	0.84–1.19
MACE‡ (no. of observations=92 266)	0.99	0.97	0.87–1.14
Multivariate analyses on imputed data			
Death (no. of observations=287 658)	0.96	0.31	0.88–1.04
Reinfarction (no. of observations=287 658)	1.02	0.78	0.89–1.17
Major bleeding (no. of observations=287 658)	1.01	0.98	0.90–1.11
MACE‡ (no. of observations=287 658)	0.97	0.44	0.90–1.04

CABG indicates coronary artery bypass grafting; MACE, major adverse cardiovascular event; MV; multivariable; OR, odds ratio; and PCI, percutaneous coronary intervention.

*Adjusted for age; sex; heart rate; blood pressure; family history of coronary heart diseases; ischemic ECG changes; left ventricular systolic dysfunction; history of diabetes mellitus, hypercholesterolemia, peripheral vascular disease, or hypertension; prescription of warfarin, intravenous nitrate, furosemide, aldosterone antagonist, beta blockers, angiotensin converting enzyme inhibitor/angiotensin receptor blockers, aspirin, P2Y12 inhibitor, or statins; Killip class; cardiac arrest; and coronary angiogram.

†Adjusted for age; sex; race; heart rate; blood pressure; serum creatinine level; family history of coronary heart diseases; ischemic ECG changes; left ventricular systolic dysfunction; PCI; history of diabetes mellitus, hypercholesterolemia, angina, cerebrovascular accident, peripheral vascular disease, hypertension, or smoking; admission under cardiology; warfarin; unfractionated heparin; intravenous nitrate; furosemide; calcium channel blockers; aldosterone antagonist; beta blockers; angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; aspirin; P2Y12 inhibitor; statins; Killip class; cardiac arrest; coronary angiogram; and PCI on imputed data.

‡MACE is defined as composite end point of inpatient death and reinfarction.

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Table 4. Propensity Score–Matched Analysis With Average Treatment Effects on Imputed Data

Outcome	Group	Coefficient* (95% CI)	OR* (95% CI)	*P* Value
In-hospital death (n=287 658)	Group 1: CABG naïve	Reference		
	Group 2: prior CABG	−0.0009289 (−0.0090477 to 0.00719)	0.98 (0.83–1.14)	0.82
In-hospital reinfarction (n=287 658)	Group 1: CABG naïve	Reference		
	Group 2: prior CABG	0.0023837 (−0.0016293 to 0.0063968)	1.27 (0.82–1.72)	0.24
In-hospital Major bleeding (n=287 658)	Group 1: CABG naïve	Reference		
	Group 2: prior CABG	−0.0013085 (−0.0048546 to 0.0022376)	0.92 (0.69–1.14)	0.47
In-hospital MACE† (n=287 658)	Group 1: CABG naïve	Reference		
	Group 2: prior CABG	0.001969 (−0.0070927 to 0.0110307)	1.03 (0.87–1.20)	0.67

CABG indicates coronary artery bypass grafting; MACE, major adverse cardiovascular event; and OR, odds ratio.

*Adjusted for age; sex; race; heart rate; blood pressure; serum creatinine level; family history of coronary heart diseases; ischemic ECG changes; left ventricular systolic dysfunction; history of heart failure, prior percutaneous coronary intervention, diabetes mellitus, hypercholesterolemia, angina, myocardial infarction, cerebrovascular accident, peripheral vascular disease, hypertension, smoking, or asthma/chronic obstructive pulmonary disease; admission under cardiology; prescription of low-molecular-weight heparin, warfarin, unfractionated heparin, glycoprotein IIb/IIIa inhibitor, intravenous nitrate, furosemide, calcium channel blockers, aldosterone antagonist, fondaparinux, beta blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, aspirin, P2Y12 inhibitor, or statins; Killip class; cardiac arrest; coronary angiogram; or PCI on imputed data.

†MACE is defined as composite end point of inpatient death and reinfarction.

Sensitivity Analysis

We undertook sensitivity analyses in patients with prior CABG to compare and contrast clinical characteristics and adverse outcomes in those who received PCI compared with those who received medical management only. Clinical characteristics of both cohorts are presented in Table S1, and pharmacotherapy, management strategy, and crude in-hospital clinical outcomes are presented in Table S2. Patients who received medical management were older and had greater prevalence of chronic kidney disease and severe left ventricular systolic dysfunction compared with those who received PCI. Adjusted risks of in-hospital clinical outcomes are presented in Table 5. In patients with prior CABG, we observed lower odds of inpatient mortality (OR, 0.67, 95% CI, 0.46–0.98; *P* – 0.04) in those who underwent PCI compared with those who received medical management alone (Table 5). However, the odds of in-hospital reinfarction, major bleeding, and MACE were not significantly different. In multivariate analyses, a history of prior CABG in patients with NSTEMI was independently associated with lower odds of inpatient coronary angiogram (OR, 0.91, 95% CI, 0.88–0.95; *P*<0.001) and revascularization (PCI/CABG) (OR, 0.73; 95% CI, 0.70–0.76; *P*<0.001) (Tables S3 through S4).

Information about missing data is presented in Table S5. Our study findings are summarized in Figure 4.

DISCUSSION

This large national study examines demographic and baseline clinical characteristics, pharmacotherapy, management strategies, and adverse clinical outcomes in patients with a history of CABG presenting with NSTEMI. Our study demonstrates that patients with prior CABG are older, with greater comorbid burden and present with higher GRACE score compared with patients with no prior history of CABG. Once differences in baseline characteristics and presentation were adjusted for, we observed similar odds of inpatient mortality, MACE, reintervention, and major

Table 5. Adjusted In-Hospital Clinical Outcomes in Patients With Prior CABG Who Received PCI Versus MEDICAL Management* (Medical Management is REFERENCE GROUP)

Clinical Outcomes	Adjusted OR* as Compared With Reference (CABG Naïve)	*P* Value	95% CI
Death (no. of observations=25 027)	0.67	0.04	0.46–0.98
Reinfarction (no. of observations=25 027)	1.13	0.47	0.81–1.57
Major bleeding (no. of observations=25 027)	1.07	0.68	0.79–1.44
MACE† (no. of observations=25 027)	0.94	0.63	0.73–1.21

CABG indicates coronary artery bypass grafting; MACE, major adverse cardiovascular event; OR, odds ratio; and PCI, percutaneous coronary intervention.

*Adjusted for age, race, heart rate, blood pressure, serum creatinine level, left ventricle systolic dysfunction, history of diabetes mellitus or cerebrovascular accident, admission under cardiology, warfarin, unfractionated heparin, glycoprotein IIb/IIIa inhibitor, intravenous nitrate, furosemide, calcium channel blockers, aldosterone antagonist, beta blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, aspirin, P2Y12 inhibitor, statins, Killip class, cardiac arrest, and coronary angiogram on imputed data.

†MACE is defined as composite end point of in-patient death and reinfarction.

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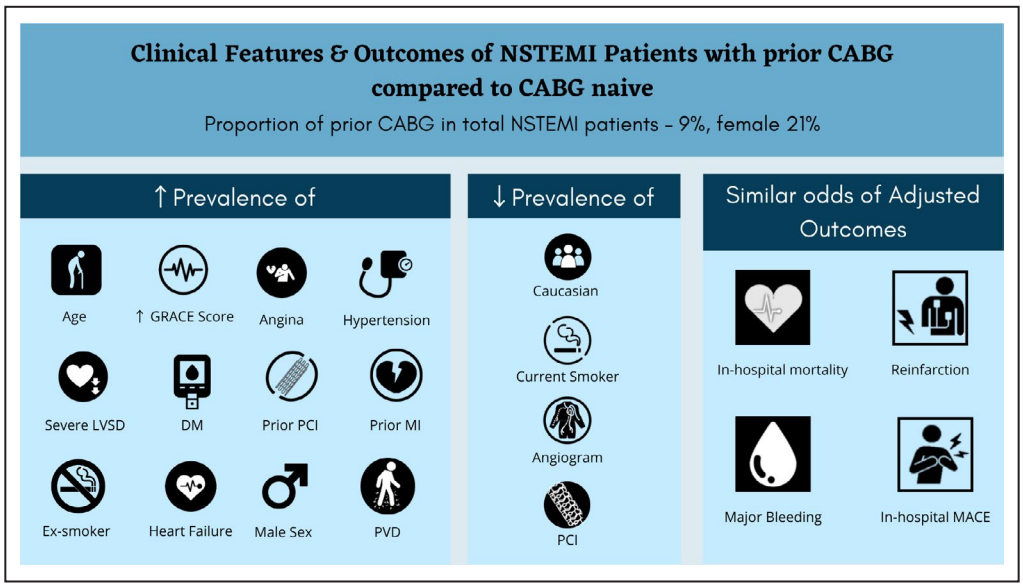

Figure 4. Clinical features and outcomes of patients with NSTEMI with prior CABG compared with CABG naïve.
CABG indicates coronary artery bypass grafting; DM, diabetes mellitus; GRACE, Global Registry of Acute Coronary Events; LVSD, left ventricular systolic dysfunction; MACE, major adverse cardiovascular event; NSTEMI, non–ST-segment–elevation myocardial infarction; PCI, percutaneous coronary intervention; and PVD, peripheral vascular disease.

bleeding between the 2 groups. However, sensitivity analysis of the patients with prior CABG who received PCI showed they had better-adjusted clinical outcomes for in-hospital all-cause mortality compared with those who received medical management, despite the observation that patients with prior CABG were less likely to receive invasive management.

The American College of Cardiology/American Heart Association and European Society of Cardiology guidelines recommend an early invasive strategy in addition to medical therapy in patients who present with NSTEMI and have a high risk of adverse clinical outcomes.[11,25] Patients with prior CABG are considered a high-risk group, and therefore, an early invasive approach is preferred in this group. However, patients with prior CABG have actually been excluded from many of the pivotal clinical trials like RITA3 (Randomized Intervention Trial of Unstable Angina 3) and Value of First Day Angiography/Angioplasty In Evolving Non-ST segment Elevation Myocardial Infarction: An Open Multicenter Randomized Trial,[31–35] which assess revascularization against medical management. In other studies, too, only small numbers of patients with prior CABG were present in acute coronary syndrome (ACS) trials (LIPSIA-NSTEMI [Leipzig Immediate Versus Early and Late Percutaneous Coronary Intervention Trial in NSTEMI]: 41/600, Italian elderly ACS; After Eighty study: 76/457; OASIS-5 [Fifth Organization to Assess Strategies in Ischemic Syndromes]: 1643/20 078).[10,36–40] Apart from a recently published pilot randomized controlled trial, in which Lee et al[22] described 24 months' outcome data of 60 patients with prior CABG (invasive group, n=31; medical group, n=29), no major clinical trials specifically examined clinical outcomes of invasive versus medical approach in patients with prior CABG who presented with NSTEMI.. During 2 years of follow-up (median, 744 days; interquartile range, 570–853), the composite outcome for efficacy (all-cause mortality, rehospitalization for refractory ischemia/angina, MI, hospitalization for HF) occurred in 13 (42%) patients in the invasive group and 13 (45%) in the medical group (HR, 0.85; 95% CI, 0.39–1.83). Five patients died in the invasive group and 3 in the medical management group. Because of the small sample size, it is not possible to provide recommendations about treatment strategies on the basis of this study. Thus, given the exclusion or underrepresentation of patients with prior CABG in pivotal NSTEMI clinical trials, current guidelines are not genuinely based upon good evidence compared with patients with NSTEMI who have never had CABG. Our current analysis helps to address this evidence gap through data analysis of a large real-world national registry.

In the present study, patients with prior CABG were less likely to receive invasive coronary angiography, even once differences in baseline characteristics were adjusted for. There are many potential explanations for this observation. For example, patients with prior CABG often have a greater burden of comorbid illnesses and have more complex and extensive disease in native

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coronary arteries and bypass grafts, which may make such patients less attractive for selective invasive management.[41] Our findings are similar to those reported by the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With EarlyImplementation Quality Improvement Initiative, which demonstrated that higher-risk patients are less likely to receive invasive management despite a greater possible benefit from a more aggressive therapeutic approach.[42] Because of more widespread availability of computed tomography coronary angiography in recent years, it is possible that some of the patients with prior CABG underwent a computed tomography coronary angiogram instead of invasive coronary angiography, and were subsequently not offered an invasive approach because of unfavorable anatomy or patent grafts.

In our study, revascularization, which was mainly in the form of PCI, was also less likely to be performed in patients with prior CABG. This corresponds to the previous observation that they were less likely to undergo invasive angiography and is likely to reflect concerns by clinicians about procedural risks relating to advanced age, higher comorbidity, well-documented higher complication rates, and a lack of clear evidence of benefit in the CABG cohort.[9,43] There might be a group of the patients who received assessment of viable myocardium with noninvasive imaging, or who underwent a computed tomography coronary angiogram/invasive coronary angiogram, and were not considered for revascularization because of either the absence of viability or flow-limiting lesions suitable for PCI. Despite using modern drug-eluting stent platforms and adjuncts like embolic protection devices, long-term outcomes of SVG PCI are suboptimal. The probability of no-reflow and periprocedural MI are found to be higher in PCI to SVG compared with native-vessel PCI in many studies.[9,44] Moreover, bypass grafts accentuate the progression of atherosclerosis and calcification in native coronary vessels with up to two-fifths of bypassed native arteries developing chronic total occlusions after 1 year of surgery.[7] Certainly, PCI to either SVGs or in native coronary arteries in patients with prior CABG are technically more challenging compared with procedures undertaken in patients without a prior history of CABG. These observations may add to the uncertainties about performing complex PCI when the procedural risk may be perceived to be higher than any potential benefits associated with an invasive approach, with medical management opted for.

In multivariate and propensity score matching analyses, we found the odds of in-hospital mortality, major bleeding, reinfarction, and MACE were similar between patients with and without prior CABG. These findings are consistent with previously published data by Kim et al[41] and Teixeira et al.[1] In an analysis of 47 557 patients with NSTEMI (prior CABG, 8790), Kim and colleagues reported no significant differences in inpatient mortality (OR, 0.99; 95% CI, 0.87–1.11) and bleeding (OR, 1; 95% CI, 0.92–1.11). Similarly, Teixeira et al reported similar adjusted odds in-hospital mortality (9.5% versus 5.9%; *P*=0.2), or mortality at 1 year (9.8% versus 9.1; *P*=0.84), major adverse cardiac and cerebrovascular events at 1 year (22 versus 17%; *P*=0.37) and almost 50% of patients underwent an invasive coronary angiogram during hospital admission. Unlike the present analysis, neither of these studies analyzed the effect of PCI on adverse clinical outcomes in patients with prior CABG.

Our analysis reports lower adjusted odds of in-hospital mortality in those patients with prior CABG who underwent PCI compared with those who managed conservatively without any additional risk of major bleeding or reinfarction. However, patients with prior CABG who received PCI had a more favorable risk profile, and it might therefore be possible that some unmeasured confounders may have contributed to worse outcomes in the medically managed cohort. Furthermore, there might be a subset of patients with prior CABG who were older with a heavy burden of comorbid illnesses, and clinicians considered them not suitable for PCI. Nevertheless, this finding might be important from a clinical perspective, as PCI was underused in patients with NSTEMI who had a prior history of CABG in almost all of the previously published data and in present study, though it was associated with a mortality benefit compared with conservative management.[41] These results may provide insight to clinicians around the utility of an invasive management approach in this high-risk and complex cohort of patients. Prospective, randomized controlled clinical trials are now needed to test the validity of these observational results.

Strengths and Limitations

This large national-level study is the first to provide a broad overview of real-world practice of management strategies, temporal changes, and adverse clinical outcomes of patients with a history of prior CABG and presenting with NSTEMI ACS. The MINAP data set comprises an almost complete record of all patients with NSTEMI admitted in the United Kingdom representing the largest real-world experience of this cohort of patients, containing high-risk patients with multiple comorbid illnesses that are often not included or underrepresented in clinical trials. The large sample size of this national study gives us sufficient statistical power to detect differences in adverse clinical outcomes between the 2 cohorts of interest.

Despite having several strengths, certain limitations should be considered while interpreting our study observations. A key inherent limitation of the current study was that it was based on retrospective analysis

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of prospectively collected data of a national registry and therefore was subject to all the limitations of observational studies. Second, although the MINAP data set included many important clinical and demographic variables of interest, much valuable additional information like procedural details, operator experience, details about culprit vessels, infarct size, information about imaging investigations like computed tomography coronary angiography and cardiac magnetic resonance, and lesion characteristics are not routinely collected. Third, MINAP records only in-hospital clinical outcomes, and it is possible that long-term follow-up data may reveal differences in clinical outcomes between PCI and medically managed patients with prior CABG. Fourth, time-of-death data are not available in MINAP, and there is a possibility that some patients died during first few hours of admission without getting assessment for a PCI, leading to an immortal time bias that may account for the more favorable outcomes for those patients managed with PCI. Fifth, MINAP does not record information about whether PCI was undertaken in the native vessel or in vein grafts in patients with prior CABG. Our previous work around this theme, derived from the British Cardiovascular Intervention Society data set, suggests that outcomes are similar once differences in baseline characteristics are adjusted for.[45] Finally, it is not clear from the MINAP data set whether the NSTEMI event was attributable to a ruptured plaque in either the bypass graft or native coronary artery, which may impact on management strategy and clinical outcomes differently.

CONCLUSIONS

Our study demonstrates that ≈1 in 11 patients who present with NSTEMI ACS have a history of prior CABG. The odds of receiving an invasive coronary angiogram and revascularization remained low in the patients with prior CABG even after adjustment of baseline differences. Once differences in baseline characteristics were adjusted for, we report no significant differences in in-hospital MACE, reinfarction, mortality, and major bleeding between patients with prior CABG and patients without prior CABG who presented with NSTEMI ACS. Our analysis suggests lower odds of in-hospital mortality in patients with prior CABG who were managed with PCI compared with those managed medically, without increased odds of major bleeding. This may suggest that an invasive approach may be associated with better outcomes in patients with prior CABG, although adequately powered randomized controlled clinical trials are needed to confirm these findings.

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None.

Supplementary Material

Tables S1–S5

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Supplemental Material

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Table S1. Clinical characteristics of Prior CABG patients who received PCI vs Medical management*

Variables	Missing data	No PCI (11,476)	Received PCI (7,503)	P-value
Mean age in years (SD)	0	77 (70 -82)	73 (66 – 79)	<0.001
Women (%)	0	2,560/11,476 (22%)	1,294/7,503 (17%)	<0.001
Caucasians (%)	1,573	9,539/10,544 (90%)	5,898/6,862 (86%)	<0.001
Mean BMI (SD)	16,862	28 (5)	29 (12)	0.0001
Killip class				
No Heart failure (%)	6,820	4,883/7,044 (69%)	4,047/5,115 (79%)	<0.001
Basal crepitations (%)	6,820	1,561/7,044 (22%)	775/5,115 (15%)	<0.001
Pulmonary oedema (%)	6,820	561/7,044 (8%)	253/5,115 (5%)	<0.001
Cardiogenic shock (%)	6,820	39/7,044 (0.55%)	40/5,115 (0.78%)	0.12
GRACE score				
High risk GRACE score >140 (%)	7,220	6,111/6,820 (90%)	4,054/4,939 (82%)	<0.001
Intermediate risk GRACE score 109-140 (%)	7,220	620/6,820 (9%)	732/4,939 (15%)	<0.001
Low risk GRACE score <109 (%)	7,220	89/6,820 (1%)	153/4,939 (3%)	<0.001
Other clinical characteristics				
ECG ST changes (%)	471	8,960/11,194 (80%)	5,691/7,314 (78%)	<0.001
Previous smoker (%)	966	8,899/18,979 (47%)	5,329/10,773 (49%)	<0.001
Current smoker (%)	966	2,111/18,979 (5%)	1,163/10,773 (11%)	<0.001
Chronic renal failure (%)	374	1,884/11,275 (17%)	787/7,330 (11%)	<0.001
Prior percutaneous coronary intervention (%)	328	2,867/11,277 (25%)	2,765/7,374 (38%)	<0.001
Diabetes (%)	180	4,723/11,380 (42%)	3,092/7,419 (42%)	0.81
CCF (%)	397	1,848/11,264 (16%)	731/7,318 (10%)	<0.001
Hypercholesterolemia (%)	525	5,088/11,153 (46%)	4,157/7,301 (57%)	<0.001
Previous MI (%)	299	7,237/11,297 (64%)	4,819/7,383 (65%)	0.09
Angina (%)	344	7,481/11,289 (66%)	4,985/7,346 (68%)	0.02
Cerebrovascular disease (%)	340	1,699/11,311 (15%)	794/7,328 (11%)	<0.001

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Peripheral vascular disease (%)	443	1,273/11,229 (11%)	749/7,307 (10%)	0.02
Hypertension (%)	221	7,072/11,351 (62%)	5,069/7,407 (68%)	<0.001
Asthma / COPD (%)	325	2,084/11,313 (18%)	1,161/7,341 (16%)	<0.001
Family history of CAD (%)	3,652	2,258/9,102 (25%)	2,101/6,225 (34%)	<0.001
Admission under Cardiologist (%)	723	5,461/10,972 (50%)	2,623/7,284 (36%)	<0.001
Mean heart rate, bpm (SD)	1,458	80 (22)	75 (20)	<0.001
Mean systolic blood pressure (SD)	3,919	139 (28)	141 (26)	<0.001
Moderate LVSD (EF 35-45%) (%)	3,846	2,081/8,984 (23%)	1,602/6,149 (26%)	<0.001
Severe LVSD (EF <35%) (%)		1,115/8,984 (12%)	520/6,149 (8%)	<0.001
Cardiac arrest (%)	379	514/11,271 (5%)	176/7,329 (2%)	<0.001

* Excluded those patients who received redo CABG and where data for PCI was missing

CABG; Coronary artery bypass grafting, PCI; Percutaneous coronary intervention, MI; Myocardial infarction, BMI; Body mass index, GRACE: Global Registry of Acute Coronary Events, ECG; Electrocardiograph, CCF; Congestive cardiac failure, COPD; Chronic obstructive pulmonary disease, CAD; Coronary artery disease, IQR; Interquartile range, LVSD; left ventricular systolic dysfunction, EF; ejection fraction, SD; Standard deviation

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Table S2. In-hospital management strategy & crude clinical outcomes in Prior CABG patients who received PCI vs Medical management*.

Variables	Missing data	CABG Naïve (n= 262,362)	Prior CABG (n=25,296)	P-value
Pharmacotherapy				
Low molecular weight heparin (%)	2,085	5,552/10,471 (53%)	3,328/6,423 (52%)	0.13
Fondaparinux (%)	2,049	4,335/10,480 (41%)	2,824/6,450 (44%)	0.002
Warfarin (%)	2,177	1,359/10,422 (13%)	578/6,380 (9%)	<0.001
Unfractionated heparin (%)	2,234	827/10,384 (8%)	1,786/6,361 (28%)	<0.001
Glycoprotein 2b/3a inhibitor (%)	1,870	161/10,567 (2%)	433/6,542 (7%)	<0.001
IV Nitrate (%)	2,175	1,227/10,421 (12%)	1,186/6,383 (19%)	<0.001
Furosemide (%)	2,081	4,846/10,491 (46%)	2,018/6,407 (32%)	<0.001
Calcium channel blockers (%)	2,113	2,687/10,449 (26%)	1,838/6,417 (29%)	<0.001
IV beta blockers (%)	2,083	113/10,484 (1%)	70/6,412 (1%)	0.93
MRA (%)	2,295	1,407/10,322 (14%)	563/6,362 (9%)	<0.001
Thiazide diuretics (%)	2,227	524/10,390 (5%)	329/6,362 (5%)	0.72
Aspirin (%)	33	10,942/11,451 (96%)	7,391/7,495 (99%)	<0.001
P2Y12 inhibitor (%)	58	10,389/11,437 (91%)	7,284/7,484 (97%)	<0.001
Statins (%)	73	10,444/11,452 (91%)	6,993/7,454 (94%)	<0.001
ACE inhibitors/ARB (%)	64	9,520/11,455 (83%)	6,595/7,460 (88%)	<0.001
Beta-Blockers (%)	113	9,379/11,429 (82%)	6,342/7,437 (85%)	<0.001
Management strategy				
Radionuclide Study (%)	1,948	420/10,489 (4%)	134/6,542 (2%)	<0.001
Exercise test (%)	1,680	283/10,657 (3%)	323/6,642 (5%)	<0.001
Coronary angiogram (%)	754	5,344/11,084 (48%)	7,141/7,141 (100%)	<0.001
Crude in-hospital clinical outcomes				
Death (%)	0	740/11,476 (6%)	78/7,503 (1%)	<0.001
Cardiac mortality (%)	0	617/11,476	67/7,503	<0.001

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		(5%)	(1%)	
Reinfarction (%)	796	137/11,070 (1%)	81/7,113 (1%)	0.55
Major bleeding (%)	289	222/11,335 (2%)	106/7,355 (1%)	0.009
MACE * (%)	0	841/11,476 (7%)	156/7,503 (2%)	<0.001

CABG; Coronary artery bypass grafting, IV; Intravenous, MRA; Mineralocorticoid receptor antagonist, ACE; angiotensin converting enzyme inhibitor, ARB; angiotensin receptor blockers, MACE; Major adverse cardiovascular events

∗ MACE is defined as composite endpoint of in-patient death and reinfarction

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Table S3. Odds of receiving in-patient coronary angiogram in prior CABG patients in Multivariate analysis (reference: CABG naïve) (number of observations = 287,658).

Variables	Odds Ratio	P-value	Lower bound 95% CI	Upper bound 95% CI
Prior CABG	0.91	<0.001	0.88	0.95
Age	0.92	<0.001	0.92	0.95
Female	0.63	<0.001	0.61	0.64
Heart rate	0.992	<0.001	0.991	0.993
BMI	1.016	<0.001	1.011	1.021
Blood pressure	1.006	<0.001	1.005	1.007
Creatinine level (mmol/l)	0.997	<0.001	0.996	0.998
Family history of CAD	1.48	<0.001	1.43	1.53
Caucasians	1.28	<0.001	1.22	1.34
ECG changes	0.91	<0.001	0.89	0.94
Severe LVSD	0.81	<0.001	0.80	0.81
Heart failure	0.71	<0.001	0.68	0.74
Prior PCI	1.58	<0.001	1.52	1.64
DM	0.88	<0.001	0.86	0.90
Hypercholesterolaemia	1.37	<0.001	1.33	1.40
Angina	0.87	<0.001	0.84	0.88
Prior MI	0.69	<0.001	0.67	0.71
Prior CVA	0.61	<0.001	0.59	0.63
PVD	0.90	<0.001	0.86	0.94
Hypertension	1.04	0.003	1.01	1.06
Smoking	0.99	0.38	0.98	1.01
Asthma/COPD	0.89	<0.001	0.87	0.91
Admission under cardiology	0.58	<0.001	0.57	0.59
LMWH	1.09	<0.001	1.06	1.12
Warfarin	0.99	0.86	0.94	1.05
Unfractionated heparin	4.37	<0.001	4.18	4.58
Glycoprotein 2b/3a antagonist	2.35	<0.001	2.12	2.60
IV nitrate	1.37	<0.001	1.31	1.43
Furosemide	0.61	<0.001	0.59	0.63
Calcium channel blockers	1.03	0.06	0.99	1.05
MRA	0.91	<0.001	0.87	0.96
Fondaparinux	1.21	<0.001	1.18	1.24
Radionuclide Study	0.48	<0.001	0.45	0.52

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Exercise test	0.98	0.67	0.92	1.05
Reinfarction	0.90	0.07	0.81	1.01
Major bleeding	0.60	<0.001	0.56	0.65
Betablockers	1.28	<0.001	1.24	1.32
ACEI/ARB	1.59	<0.001	1.55	1.64
Aspirin	1.64	<0.001	1.53	1.75
P2Y12 inhibitor	1.99	<0.001	1.92	2.08
Statins	0.89	<0.001	0.86	0.92
Killip class	0.73	<0.001	0.71	0.75
Cardiac arrest	0.45	<0.001	0.42	0.48
Cardiogenic shock	4.09	<0.001	3.3	5.1
Pulmonary oedema	1.33	<0.001	1.23	1.44

CABG; Coronary artery bypass grafting, PCI; Percutaneous coronary intervention, MI; Myocardial infarction, BMI; Body mass index, GRACE: Global Registry of Acute Coronary Events, ECG; Electrocardiograph, CCF; Congestive cardiac failure, COPD; Chronic obstructive pulmonary disease, CAD; Coronary artery disease, LVSD; left ventricular systolic dysfunction, EF; ejection fraction, IV; Intravenous, MRA; Mineralocorticoid receptor antagonist, ACE; angiotensin converting enzyme inhibitor, ARB; angiotensin receptor blockers

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Table S4. Odds of receiving in-patient revascularization (PCI/CABG) in prior CABG patients in Multivariate analysis (reference: CABG naïve) (number of observations = 287,658).

Variables	Odds Ratio	P-value	Lower bound 95% CI	Upper bound 95% CI
Prior CABG	0.73	<0.001	0.70	0.76
Age	0.971	<0.001	0.971	0.972
Female	0.60	<0.001	0.59	0.62
Heart rate	0.992	<0.001	0.991	0.993
BMI	1.02	<0.001	1.01	1.03
Blood pressure	1.004	<0.001	1.003	1.005
Creatinine level (mmol/l)	0.998	<0.001	0.997	0.999
Family history of CAD	1.30	<0.001	1.26	1.33
Caucasians	1.17	<0.001	1.13	1.21
ECG changes	1.06	<0.001	1.03	1.08
Severe LVSD	0.94	<0.001	0.93	0.95
Heart failure	0.77	<0.001	0.73	0.81
Prior PCI	1.33	<0.001	1.28	1.37
DM	0.99	0.54	0.97	1.01
Hypercholesterolaemia	1.36	<0.001	1.33	1.39
Angina	0.94	<0.001	0.92	0.96
Prior MI	0.71	<0.001	0.69	0.73
Prior CVA	0.71	<0.001	0.69	0.74
PVD	1.02	0.38	0.98	1.03
Hypertension	0.99	0.38	0.97	1.01
Smoking	1.07	<0.001	1.06	1.09
Asthma/COPD	0.94	<0.001	0.91	0.96
Admission under cardiology	0.66	<0.001	0.64	0.67
LMWH	1.007	0.53	0.98	1.03
Warfarin	0.78		0.73	0.82
Unfractionated heparin	2.64	<0.001	2.57	2.72
Glycoprotein 2b/3a antagonist	2.40	<0.001	2.25	2.56
IV nitrate	1.24	<0.001	1.20	1.29
Furosemide	0.67	<0.001	0.64	0.69
Calcium channel blockers	0.94	<0.001	0.91	0.96
MRA	0.86	<0.001	0.81	0.89
Fondaparinux	1.02	0.08	0.99	1.04
Radionuclide Study	0.49	<0.001	0.46	0.52

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Exercise test	1.09	<0.001	1.03	1.14
Reinfarction	1.09	0.13	0.97	1.21
Major bleeding	0.98	0.58	0.91	1.05
Betablockers	1.24	<0.001	1.20	1.28
ACEI/ARB	1.37	<0.001	1.34	1.42
Aspirin	1.64	<0.001	1.54	1.75
P2Y12 inhibitor	1.98	<0.001	1.90	2.07
Statins	1.06	<0.001	1.03	1.09
Killip class	0.75	<0.001	0.73	0.78
Cardiac arrest	0.67	<0.001	0.63	0.71
Cardiogenic shock	3.87	<0.001	3.26	4.60
Pulmonary oedema	1.41	<0.001	1.29	1.53

CABG; Coronary artery bypass grafting, PCI; Percutaneous coronary intervention, MI; Myocardial infarction, BMI; Body mass index, GRACE: Global Registry of Acute Coronary Events, ECG; Electrocardiograph, CCF; Congestive cardiac failure, COPD; Chronic obstructive pulmonary disease, CAD; Coronary artery disease, LVSD; left ventricular systolic dysfunction, EF; ejection fraction, IV; Intravenous, MRA; Mineralocorticoid receptor antagonist, ACE; angiotensin converting enzyme inhibitor, ARB; angiotensin receptor blockers

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Table S5. Information about Missing data.

Variables	Missing data
Age (years)	0
Women	0
Caucasians	23,963
BMI median	254,976
No Heart failure	101,452
Basal crepitations	101,452
Pulmonary oedema	101,452
Cardiogenic shock	101,452
High risk GRACE score >140	106,891
Intermediate risk GRACE score 109-140	106,891
Low risk GRACE score <109	106,891
ECG ST changes	7,106
Previous smoker	13,712
Current smoker	13,712
Chronic renal failure	2,795
Prior percutaneous coronary intervention	1,283
Diabetes	2,362
CCF	2,901
Hypercholesterolemia	5,552
Previous MI	1,733
Angina	3,173
Cerebrovascular disease	2,336
Peripheral vascular disease	3,392
Hypertension	1,731
Asthma / COPD	2,251
Family history of CAD	47,816
Admission under Cardiologist	12,634
Heart rate, bpm, median	20,255
Systolic blood pressure	56,759
Moderate LVSD (EF 35-45%)	60,673
Severe LVSD (EF <35%)	60,673
Cardiac arrest	6,205
Low molecular weight heparin	27,945
Fondaparinux	26,848
Warfarin	29,133
Unfractionated heparin	29,892
Glycoprotein 2b/3a inhibitor	25,556
IV Nitrate	29,186
Furosemide	28,527
Calcium channel blockers	28,941
IV beta blockers	27,892
MRA	30,855
Thiazide diuretics	29,572
Aspirin	790

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P2Y12 inhibitor	1,190
Statins	1,528
ACE inhibitors/ARB	1,300
Beta-Blockers	2,712
Management strategy	
Radionuclide Study	29,011
Exercise test	24,847
Coronary angiogram	12,670
Percutaneous coronary intervention	65,557
CABG	65,557
Revascularization (CABG/PCI)	65,557
Crude in-hospital clinical outcomes	
Death	0
Cardiac mortality	0
Reinfarction	12,859
Major bleeding	5,014
MACE*	0

CABG; Coronary artery bypass grafting, PCI; Percutaneous coronary intervention, MI; Myocardial infarction, BMI; Body mass index, GRACE: Global Registry of Acute Coronary Events, ECG; Electrocardiograph, CCF; Congestive cardiac failure, COPD; Chronic obstructive pulmonary disease, CAD; Coronary artery disease, LVSD; left ventricular systolic dysfunction, EF; ejection fraction, IV; Intravenous, MRA; Mineralocorticoid receptor antagonist, ACE; angiotensin converting enzyme inhibitor, ARB; angiotensin receptor blockers, MACE; Major adverse cardiovascular events

* MACE is defined as composite endpoint of in-patient death and reinfarction

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